PMA Memorandum

Subject: M020022/M002: Non-clinical testing

Device: X STOP Interspinous Process Distraction System ("X STOP")

Indications: The X STOP is indicated for patients aged 50 or older suffering from intermittent

neurogenic claudication secondary to mild to moderate lumbar spinal stenosis at one

or two levels, and who have undergone a regimen of non-operative treatment.

Sponsor: St. Francis Medical Technologies, Inc.

Contact: Yvonne Lysakowski

Vice President, Clinical and Regulatory Affairs

Device Description

The X STOP Interspinous Process Distraction System is manufactured from Ti 6Al-4V ELI titanium alloy that conforms to ASTM Standard F136-96 (Standard Specification for Wrought Titanium-6 Aluminum-4 Vanadium ELI (Extra Low Interstitial) Alloy (R56401) for Surgical Implant Applications). The device consists of two components: a spacer assembly and a wing assembly. The spacer assembly is comprised of a tissue expander, a fixed wing, and an oval spacer. The wing assembly is comprised of an adjustable wing and locking screw. After the spacer assembly is implanted, the wing assembly is attached, the width is adjusted, and the screw tightened with a torque-limiting hex-head screwdriver. The proposed principal behind the X STOP is that by distracting symptomatic spine segments and maintaining them in a slightly flexed position, symptoms of lumbar spinal stenosis can be relieved. (Note: In Amendment 3 of the PMA, the device is referred to as the X STOP Interspinous Process *Decompression* System.)

The X STOP is available in five sizes, with the size referring to the minor diameter of the oval spacer in the spacer assembly. (Engineering drawings are available in Attachment 2.1 of Module 2.)

<u>Model</u>	<u>Description</u>
1-1206	6mm X STOP Interspinous Process Distraction System
1-1208	8mm X STOP Interspinous Process Distraction System
1-1210	10mm X STOP Interspinous Process Distraction System
1-1212	12mm X STOP Interspinous Process Distraction System
1-1214	14mm X STOP Interspinous Process Distraction System

The device is implanted using an instrument set designed to work with the X STOP; it includes the following items:

- 1. Small dilator
- 2. Large dilator
- 3. Distractor
- 4. Spacer insertion instrument
- 5. Wing insertion instrument
- 6. Hex head screwdriver

Design versions

An original design of the implant device was used in a ten-patient pilot study from May of 1997 to April of 1998. An "unwelded" version of the device, in sizes up to 12mm, was implanted in 22 patients in a clinical trial that began in February 2000. The sponsor stopped the study in May 2000, after 5 device failures (loosening / disassembly of the Threaded Insert and Tissue Expander components) in the 22 study patients implanted with the device. Following a failure investigation that included testing of devices still in inventory, a manufacturing step was added to laser weld the Threaded Insert in place, to prevent the implant from disassembling once implanted. Additional, subsequent design modifications included an increased taper angle of the Tissue Expander, a more rounded Tissue Expander tip, redesign of the Threaded Insert / Tissue Expander connection, a modified Universal Wing design to allow for improved mating with the modified tissue expander, and a larger 14mm size. *The pivotal study trial was conducted using this modified, "welded" version of the implant.*

Conformance to Performance Standards

The sponsor cites several standards to which it conforms:

ASTM F136-96: Wrought Titanium-6 Aluminum-4 Vanadium ELI (Extra Low Interstitial) Alloy (R56401) for Surgical Implant Applications

ASTM F2077-01: Test Methods for Intervertebral Body Fusion Devices

EN 1441: Medical Devices - Risk Analysis

EN 46001 Application of ISO 9001 to the Manufacture of Medical Devices

ISO 9001 Quality System

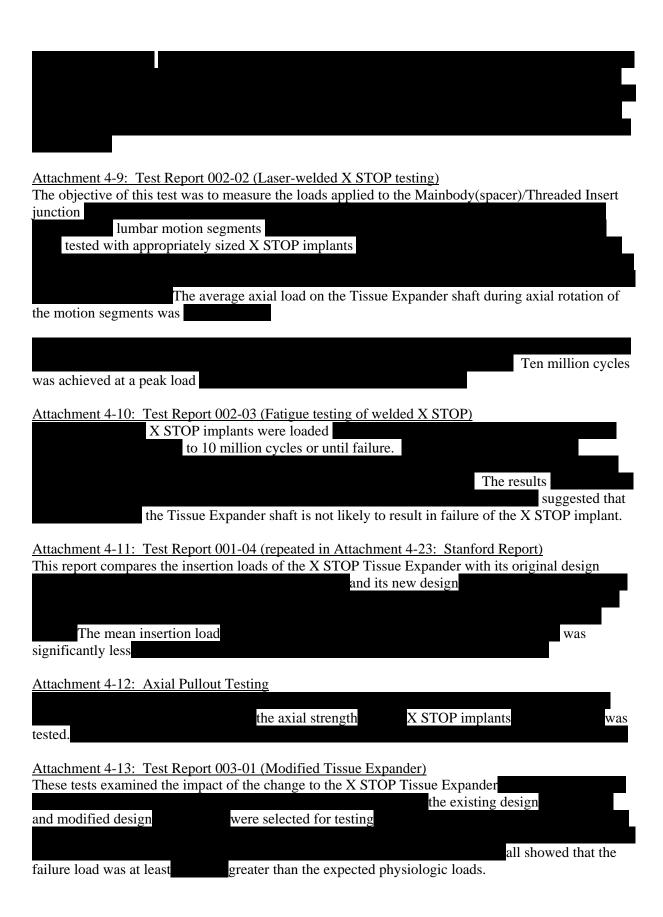
Pre-clinical Testing

Much of the pre-clinical testing was performed on the original, unwelded version of the device. Following the changes leading to the welded design, additional testing was performed to validate the new design. The test reports have been separated by the sponsor into two groups: mechanical and biomechanical. The mechanical tests include both static and fatigue tests to characterize the X STOP and determine its ultimate strength. The biomechanical tests were conducted to understand the relationship between the loads required to implant the X STOP, the *in vivo* loads experienced by the X STOP, and spinous process failure loads. Tests were also performed to evaluate the stability of the implanted X STOP when it is subjected to extreme loads. The test reports are included in a series of 32 attachments to section 4 (Non-Clinical Laboratory Studies) in M020022 Module 2.

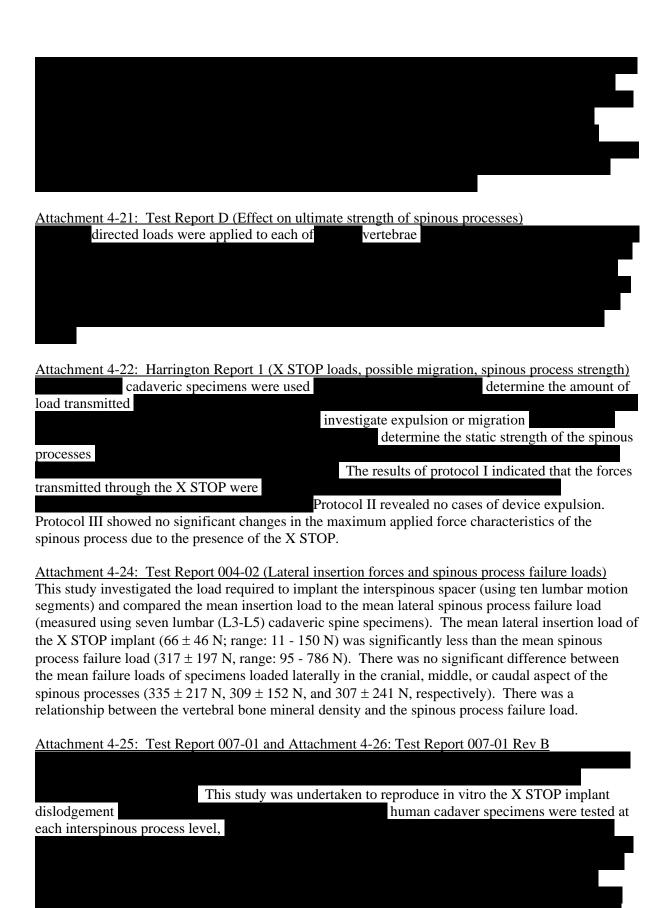
FDA sent the sponsor a letter dated January 30, 2003, requesting additional information. Responses were submitted by the sponsor in a module amendment, M020022/M002/A001. Following review of the responses, FDA sent the sponsor a letter dated September 22, 2003, indicating that the module is accepted and is now considered closed.

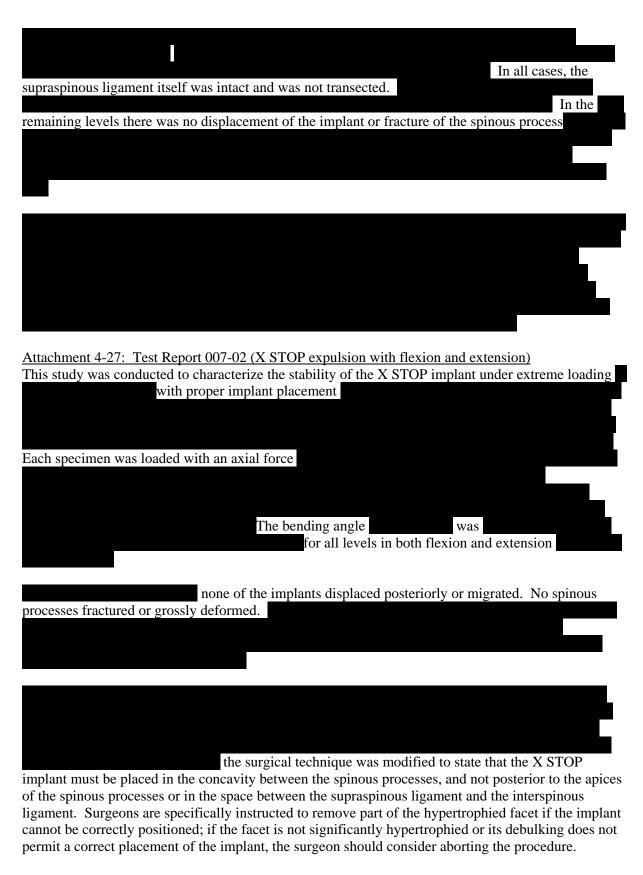
The pre-clinical test reports submitted in Module 2 are briefly summarized below. The full test reports can be found in Binder 3 of the panel pack. The results in the test reports in Attachments 4-30 and 4-31 are part of the topic of FDA questions for the panel.

Attachment 4-1: Test Report B (Fatigue test)	
This report includes cyclic compression fatigue loa	
The peak compressive	
X STOP spacers ran out to 10 million cycles wi	
	in the original X STOP assembly the side screw
and the end screw. The results indicated that comp	
torque.	Finally, a finite elemen
analysis was also conducted on the Universal Wing	g component.
Attachments 4-2 through 4-5: Test Reports 001, 00)1-01_001-02_001-03 (Explant analyses)
	X STOP implants, as well as sample implants of the
same original design, to determine the cause of the	· · · · · · · · · · · · · · · · · · ·
Attachment 4-6: Test Report 004-01 (Insertion for	
This study was undertaken to measure the loads im insertion in a cadaver model.	parted on an X STOP implant during manual
insertion in a cadaver moder.	
Attachment 4-7: Test Report 002 (Laser-welded X	STOP testing)
This report describes testing of the laser welded X	STOP
Axial tensile load tests were conducted	
Axiai tenshe load tests were conducted	
	1
The test concluded that laser welding does	s not alter the tensile mechanical properties of the
assembly.	
"Endurance tests" were conducted	
	The peak compressive loads were
The X STOP devices	ashiaved run out to 10 million avales
without failure.	achieved run out to 10 million cycles
without failure.	
Torque release testing was performed	
	there was no cracking or
visual change evident at the weld	
Cimpulated incomtion toots and death as11-	A V STOD
Simulated insertion tests were conducted on welder	1 V 210L

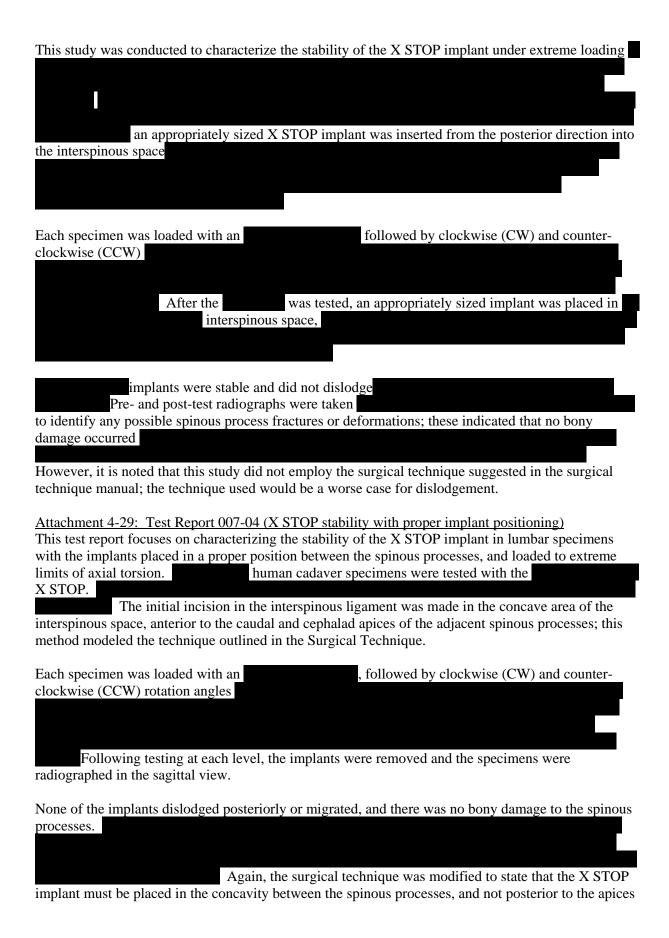


Attachment 4-14: Test Report 003-04 (Modified Universal Wing) The purpose of these tests was to evaluate the static and fatigue characteristics
Attachment 4-15: Test Report 008-01 (FEA of 14mm X STOP) A finite element analysis was performed on the X STOP implant.
Attachment 4-16: Test Report 003-02 (Modified engagement of Tissue Expander shaft and Spacer) This test report evaluated the static and fatigue loading characteristics the Tissue Expander shaft with the Main Body
Attachment 4-17: Test Report 003-03 (Modified Threaded Insert) A series of tests were conducted to evaluate the effects of modifications to improve the manufacturability of the laser weld process. The following static tests were performed on the modified X STOP and compared to similar testing
Attachment 4-18: Test Report C (In vitro loads on spacer) Data on expected in vivo loads between the spinous processes were measured during biomechanical testing at the University of Washington Biomechanical Lab.
Attachment 4-19: Test Report A (In vitro loads vs spinous process failure strength) An in vitro test was performed using X STOP spacers fitted implanted into cadaveric lumbar motion segments.
Attachment 4-20: Test Report 005-01 (In vitro loads vs spinous process failure strength) The objective of these tests was to measure the in situ loads of an interspinous spacer, and relate these to the spinous process failure loads measured
Each specimen was then disarticulated into individual vertebrae





Attachment 4-28: Test Report 007-03 (X STOP expulsion with axial torsion)



of the spinous processes or in the space between the supraspinous ligament and the interspinous ligament.

Attachment 4-30: Test Report 016-01 (Effect of X STOP on spinal and foramen dimensions)
The purpose of this study was to quantify the effect of the implant on the canal areas during flexion and extension. The sponsor hypothesized that, in extension, the canal area of the treated level would be greater than that of the intact specimen, and unaffected during flexion. They also hypothesized that the adjacent canal areas would be unaffected by the implant

Eight lumbar cadaver specimens (L2-L5) were placed in a custom acrylic frame capable of placing the specimens in a 1) neutral position, 2) 15° of flexion, or 3) 15° of extension. Once in the positioning frame, the specimens were placed in a 1.5 Tesla MRI scanner. Specimens were scanned in three positions (flexion, neutral, and extension) with and without the X STOP implant placed at the L3-L4 interspinous space. Axial slices were used to measure: 1) the canal area, 2) the lateral recess distance, and 3) the A/P canal depth at the L2/3, L3/4, and L4/5 levels. In addition, para-sagittal slices were used to measure: 1) the foramen area, 2) the foramen height, and 3) the foramen width at the L2/3, L3/4, and L4/5 levels.

<u>Canal Area</u>: At the L2-3 and L4-5 levels, there was no difference in the mean canal area between the intact and X STOP implanted specimens for a given position. The mean canal area did, however, decrease from flexion to extension for both the intact and implanted specimens. At the L3-4 level in the neutral and extended positions, the mean canal area of the X STOP implanted specimens was significantly greater than that of the intact specimens; there was no difference in flexion. Implanting the X STOP increased the mean area of the canal in extension by 18% (2.31 cm² to 2.73 cm²).

<u>Canal Diameter</u>: Similar to the canal areas, there was no difference in the mean mid-sagittal canal diameter between the intact and X STOP implanted specimens for a given position at the L2-3 and L4-5 levels. The mean canal diameter did decrease from flexion to extension for both the intact and implanted specimens. At the L3-4 level extended position, the mean canal area of the X STOP implanted specimens was significantly greater than that of the intact specimens; there was no difference in flexion or neutral.

<u>Subarticular Diameter</u>: Similar to the previous two measurements, there were no differences in the mean subarticular diameter at the L2-3 or L4-5 levels. At the L3-4 level, however, the X STOP increased the diameter by 14% in the neutral position and 49% in extension.

Ligamentum Flavum: There were no consistent trends at either the adjacent or treated levels.

<u>Foramen Area</u>: At the L2-3 and L4-5 levels, there was no difference in the mean foraminal area between the intact and X STOP implanted specimens for a given position. The mean area did decrease from flexion to extension for both the intact and implanted specimens. At the L3-4 level in the extended position, the mean canal area of the X STOP implanted specimens was significantly greater than that of the intact specimens; there was no difference in flexion or neutral.

<u>Foramen Height</u>: Similar to the ligamentum flavum thickness, the foraminal height was not sensitive to changes in position or treatment.

<u>Foramen Width</u>: Similar to the lateral recess height in the axial view, the foramen width in the sagittal view was sensitive to position and treatment changes; in extension, the X STOP increased the foraminal width by 41%.

All of these results are summarized in the last two columns of the table below. (The four middle columns include literature data provided by the sponsor.) The sponsor states that these tests demonstrate that the X STOP implant prevents canal narrowing at the implanted level in extension. They also state that the X STOP does not alter the dimensions of the adjacent, intact levels, in the extended, flexed or neutral positions, although this data is not presented in the sponsor's report. The table shows that, in all cases except one (foramen height), the smallest dimension was measured without the X STOP present ("Current test Intact") and with the segment in a position of extension. With the segment in an extended position, the presence of the X STOP resulted in increased dimensions. (FDA notes that in the *flexed* segment position, the presence of the X STOP resulted in *smaller* values for all of the dimensions except foramen width, although the differences are not statistically significant.)

Table 1. Published Values of canal and Foramen Dimensions										
Dimension	Position	Chung	Fujiwara	Inufusa	Schmid	Current	Current			
		(2000)	(2001)	(1996)	(1999)	test Intact	test with			
							X STOP			
Canal Area (mm ²)	Flex	399		248	268	286	276			
	Ext	331		208	224	231	273			
Canal Diameter	Flex	25.0		20.2		19.3	19.0			
(mm)	Ext	23.0		17.7		17.8	19.5			
Subarticular	Flex	5.7		5.8		4.5	4.1			
Diameter (mm)	Ext	3.2		4.7		2.5	3.7			
Lig Flay Thickness	Flex	1.8		3.5	1.8	3.0	2.9			
(mm)	Ext	2.5		2.9	4.3	2.9	2.9			
Foramen Area	Flex		104	141	167	149	147			
(mm^2)	Ext		83.9	107	115	106	133			
Foramen Height	Flex		17.9	20.0		23.2	22.4			
(mm)	Ext		18.2	20.3		21.3	21.2			
Foramen Width	Flex		4.0	5.8		5.8	6.0			
(mm)	Ext		2.2	3.5		3.4	4.8			

Attachment 4-31: Test Report 015-01 (Effect of X STOP on spinal kinematics)

A concern with the implantation of the interspinous spacer is that, by restricting flexion-extension at one motion segment level, the kinematics and loading of the adjacent levels may be altered, leading to degeneration and instability. This study investigated the use of the interspinous spacer on the kinematics of the lumbar spine. The sponsor hypothesized that the spacer will reduce the range of motion of the treated level in flexion-extension, while not affecting the treated level in axial rotation or lateral bending. They also hypothesized that the adjacent levels would not be affected.

Seven human lumbar (L2-L5) cadaver specimens were used for this testing. Each specimen was placed in a spinal loading frame capable of applying independent bending moments and axial loads. Labeled steel pins 10 cm in length were placed in each vertebra and on the upper and lower actuator to indicate the angular position. Two CCD cameras were used to record the position of the pins during the testing. Three images were taken during each test cycle: Neutral, Flexion or Left Bending/Rotation, and Extension or Right Bending/Rotation.

With a superimposed 700 N compressive force, specimens were initially tested intact by applying a \pm 7.5 Nm bending moment in flexion and extension, left and right axial rotation, and left and right lateral

bending. Angle, force and torque data were recorded for each motion. Following the intact testing, the specimens were removed from the loading frame and an appropriately sized interspinous spacer was placed between the L3-L4 spinous processes in each specimen. The specimens were returned to the loading frame and the previously described loading regimen was applied to each specimen.

There was no significant difference between the mean range of motion of the intact and X STOP implanted specimens during axial rotation and lateral bending. During flexion/extension, however, the range of motion at the implanted L3/4 level was significantly reduced. The ranges of motion at the adjacent levels were not significantly changed. The results showed that placement of the interspinous implant in the specimen results in a 2° decrease in lordosis from L2-L5.

Attachment 4-32: Test Report 014-01 (Disc pressure)

This study investigated changes to intervertebral disc pressure at the level of X STOP instrumentation and at the adjacent disc levels above and below the level of insertion. The sponsor hypothesized that placement of an interspinous implant would result in a decrease in the intervertebral disc pressure at the level of instrumentation, without significantly affecting the disc pressures at the adjacent levels.

Eight cadaver lumbar spines were obtained from donors aged 56 to 80 years and stored at -22° C. The specimens were thawed and separated into motion segments consisting of 4 vertebrae (L2-L5) and 3 corresponding vertebral discs. Before testing, a compressive force of 300 N was applied to each specimen for 15 minutes with the spines placed in the neutral position; this step was to precondition the specimens and reduce any postmortem superhydration effects of the intervertebral discs.

A pressure transducer with a diameter of 1.3 mm was placed into the appropriate disc level with the tip just through the posterior annulus to allow for stress profilometry of the respective disc. A linear variable displacement transducer was used to measure the position of the pressure transducer as it was drawn through the disc. Both transducers were located on the same apparatus, allowing for simultaneous measurements of pressure and displacement.

Initially, each motion segment was placed in the loading frame in the neutral position and subjected to an axial force of 700 N for 30 seconds, after which time the pressure transducer was pulled along the midsagittal plane of the disc being measured. Both superior and lateral components of the compressive stress were measured by rotating the transducer needle 90 degrees during successive tests. Stress profilometry was performed for each disc (L2-L5) with the specimens in neutral, flexed, and extended positions. Flexion and extension were achieved by applying a 7.5 Nm bending moment in the respective direction with a superimposed 700 N compressive force.

An appropriately sized X STOP implant was then placed between the L3 and L4 spinous processes. The sequence described above was repeated with the specimens loaded in the neutral, flexed, and extended positions. Again, a transducer measured the intradiscal pressure during loading, and a displacement transducer measured the travel of the pressure transducer through the disc.

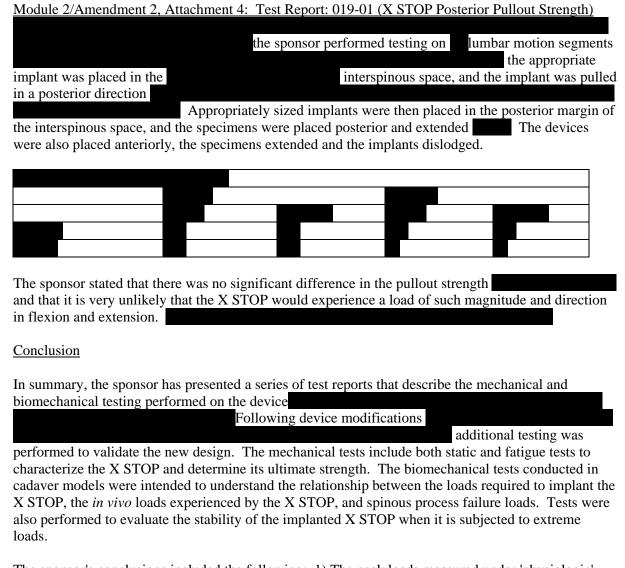
A total of 12 measurements were recorded for each disc level (6 each with and without the X STOP). The mean pressures were compared between the intact specimens and implanted specimens for a given level (L2-L3, L3-L4, L4-L5), specimen position (flexion, neutral, extension), transducer direction (superior, lateral), and disc region (posterior, nucleus, anterior). A total of 54 comparisons were made using individual paired t-tests each with a level of significance of 0.05.

As expected, the most notable differences in mean disc pressure were identified at the L3-L4 level. In extension, the mean pressure in the posterior annulus was significantly reduced with the use of the implant; the mean superior pressure was reduced by 63% and the mean lateral pressure was reduced

by 46%. The mean pressures in the region of the nucleus were significantly reduced after implantation; the mean superior pressure was reduced by 41% and the mean lateral pressure was reduced by 40%.

In the neutral position, the mean superior pressure in the posterior annulus was reduced by 38%, and the mean superior and lateral pressures in the nucleus were reduced by 20% and 17%, respectively.

There were no significant differences between the mean pressures of the intact and implanted specimens at the L2-L3 level. The only significant differences between the intact and implanted specimens at the L4-L5 were between the lateral nucleus pressures in the neutral (7%) and flexed positions (9%), and the lateral anterior annulus pressures in the extended position (12%).



The sponsor's conclusions included the following: 1) The peak loads measured under 'physiologic' loading of the spinous processes with the X STOP in place are much less than the loads to failure of the spinous processes. FDA notes that the clinical incidence of spinous process fracture should support or refute this conclusion; clinical data will also be essential in evaluating the effects of repeated loading of the spinous processes over time. 2) Proper anterior placement of the X STOP,

within the concave space of the spinous processes, is essential to preventing dislodgement of the device and/or deformation of the spinous processes. 3) The X STOP implant prevents canal narrowing at the implanted level in extension, and does not alter the dimensions of the adjacent levels in the extended, flexed or neutral positions. FDA notes that the presence of the X STOP reduces all of the spinal and foramen dimensions (except foramen width) in the flexed position, although the differences are not statistically significant. The quantitative results for the adjacent spinal levels have not been presented. 4) There is no significant difference in the mean range of motion for an intact motion segment and an X STOP implanted segment during axial rotation and lateral bending. During flexion/extension, however, the range of motion at the implanted level is significantly reduced. The ranges of motion at the adjacent levels are not significantly changed. FDA notes that these results are based on studies using cadaver specimens, and may not be indicative of changes seen clinically.

FDA welcomes comments from panel members regarding whether the clinical data support the preclinical testing conclusions related to the effects of the X STOP device on surrounding segments and/or spine biomechanics.